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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/568,148

06/09/2006

Dan Peters

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EXAMINER

RAHMANI, NILOOFAR

ART UNIT

PAPER NUMBER

1625

NOTIFICATION DATE

DELIVERY MODE

05/26/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No. 10/568,148	Applicant(s) PETERS ET AL.	
	Examiner NILOOFAR RAHMANI	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/15/2008 and 02/13/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-16 are pending and claim 17 is cancelled in the instant application.

Priority

2. This application was filed on 06/09/2006, and is a 371 of PCT/EP04/51283, filed on 06/29/2004, and claims priority of DENMARK PCT/DK03/00528, filed on 08/13/2003.

4. *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement to treat disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue”. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the

inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims.
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The instant invention is drawn to method of treatment, prevention or alleviation of a disease or a disorder or a condition of a living animal body, which disorder, disease or condition or responsive to modulation of cholinergic receptors and/or monoamine receptors, which method comprises the step of administering to such a living animal body in need thereof a therapeutically effective amount of a quinuclidine derivative of claim 1.

The state of the prior art: At the time that the invention was made, the scientific literature tends to show the speculative role of the nicotinic acetylcholine receptor and its role in the treatment of schizophrenia. "Recent studies have *suggested* that the alpha7 nicotinic acetylcholine receptor *may* play a role in the pathogenesis of schizophrenia" and "[w]e propose that alpha7 AChR may be involved in the pathophysiology of the disease and *may* serve as a reliable

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peripheral biological market in schizophrenia.” (Perl et al., The FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (2003 Oct) Vol. 17, No. 13, pp. 1948-50.)

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Nicotinic Acetyl Choline receptors (nAChR) has been linked to treat diseases such as anxiety, cognitive disorders, learning deficit, memory deficits and dysfunction, Alzheimer's disease, attention deficit, schizophrenia, Parkinson's disease, ADHD, senile dementia, etc (from the instant specification). Therefore, that many sub types of receptors have been linked to many different diseases. One ordinary skill in the art would not able to predict that which receptor can use to treat which diseases. **Amount of guidance/working examples:** Applicant provides no examples of the test compounds to treat disorders or diseases.

The breadth of the claims: The claims encompass a method of treatment, prevention or alleviation of a disease or a disorder or a condition of a living animal body, which disorder, disease or condition or responsive to modulation of cholinergic receptors and/or monoamine receptors, which method comprises the step of administering to such a living animal body in need thereof a therapeutically effective amount of a quinuclidine derivative of claim 1.

The level of the skill in the art: The level of skill in the art is high.

The quantity of experimentation needed: There are about 50 conditions listed in claim 10. Some with known pharmaceutical treatments and others without any known pharmaceutical treatments. The ability to take one condition i.e. post-traumatic syndrome and be able to treat it with a compound that inhibits acetylcholine will take undue experimentation. Then multiple that by all the conditions listed in claim 10 and all the possibilities in claim 8 would increase the undue level experimentation. Since the guidance and teaching provided by the specification is insufficient for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

Taking all of the above into consideration, it is not seen where the instant claims 8-16, for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, have been enabled by the instant specification.

4. Claims 8-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for preventing diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are

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vaccines not the compounds such as present here. In addition, it is presumed that “prevention” of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

“The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims”, *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. 1) As discussed above, preventing diseases requires identifying those patients who will acquire the disease before occurs. This would require extensive and potentially opened ended clinical research on healthy subjects. 2) The passage spanning line 35,page 70 to line 16, page71 lists the diseases Applicant intend to treat. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to medical treatment and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become afflicted before the fact. 6) The artisan using Applicants invention would be a Board Certified physician who specialized to treat diseases with an MD degree and several years of experience.

Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of disorder diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2d 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent disorders generally. That is, the skill is so low that no compound effective generally against disorders has ever been found let alone one that can prevent such conditions. 7) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by Formula (I).

The Examiner suggests deletion of the word "prevention".

5. Claim Rejections - Obvious Double Patenting

Claims 1-16 are provisionally rejected under the judicially created doctrine obviousness-type double patenting as being unpatentable over the claims 1-24 of the Us 2005/0171079 (ap # 10/772,192). Although the conflicting claims are not

identical, they are not patentably distinct from each other because the current invention embraces the invention claimed in the above patent application.

Determination of the scope and content of the prior art (MPEP §2141.01)

US 2005/0171079 claimed analogues compounds, pharmaceutical composition and method of using the compounds in claims 1-24, specifically claim 19, 17th compound (3,7-bis[(3S)-1-azabicyclo[2.2.2]octan-3-yloxy]-dibenzothiophene) as the instant claims 1-16.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02) The difference between the instant claims and the published claims is the claims are not word for word identical but the scope of both sets of claims overlaps mostly significantly with each other. For example, Y2 is a bond, and A is a group of formula (c) in the US 2005/0171079 encompasses the compounds in the instant application.

Finding of prima facie obviousness-rational and motivation (MPEP §2142.2143)

The published claims 1-24 are therefore fully embraced by the instant claims 1-16.

This is provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been issued.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 168 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/NILOOFAR RAHMANI/

05/15/2009

/Janet L. Andres/

Supervisory Patent Examiner, Art Unit 1625

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